Amendment

In the Specification

Please amend the specification as follows:

Please cancel the existing Sequence Listing for the above-identified application, replace it with the substitute Sequence Listing appended hereto, and insert at the end of the application.

At page 15, please substitute the paragraph starting at line 25 and ending on page 16, line 26, with the following paragraph:

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From the results obtained in the experiments of the invention, it may, inter alia, be concluded that Scc1p/SCC1 is the only subunit of the cohesion comples cleaved by Esp1/separin. This does, however, not exclude the possibility that other types of proteins, for example, other cohesion proteins or proteins which regulate mitotic spindles, might also be targets/substrates of separin. One way of addressing this question is to make a version of Scc1p that has one cleavage site replaced with a site for a foreign protease (with the other cleavage site removed). An example for a convenient protease to use is TEV protease (Daugherty et al., 1989), which has a very specific cleavage site (Glu-Asn-Leu-Tyr-Phe-Gln-Gly (SEQ ID NO:2)). A strain can be constructed that contains: the SCC1 gene containing a TEV protease cleavage site, a chromosomal *cdc20-3* mutation, and the TEV protease gene under *GAL1-10* inducible control. In the presence of galactose at the restrictive temperature (when *cdc20-3* cells are arrested in metaphase due to their failure to destroy Pds1), the effect of the artificial cleavage of Scc1p on its removal from chromosomes can be assayed (as measured by its presence in sedimented chromosomal DNA fractions). Whether or not this is sufficient for sister chromatid separation can also be examined microscopically, using the CenV-GFP system (Ciosk et al., 1998; see Example 3). These experiments allow to determine whether the rest of mitosis can proceed under these conditions in the absence of separin function (note that separin is inactive in cdc20-3 mutants at the restrictive temperature due to the presence of its inhibitor Pds1). If the foreign protease triggers Scc1p's dissociation from chromatids under these circumstances and sister chromatids segregate to opposite poles of the yeast cell, it can be concluded that cleavage of Scc1 is the sole function of separin needed for sister chromatid segregation. If however, sister chromatids fail to segregate to opposite poles of the cell

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despite the variant Scc1p having been removed from chromatin, then it is concluded that separin has one or more functions besides cleavage of Scc1p. A clue as to these functions can be obtained from the phenotype of these cells and this can be used to identify other potential substrates for Esp1.